

CDC Guideline for Prescribing Opioids for Chronic Pain

Debbie Dowell, MD, MPH, LCDR, USPHS

Senior Medical Advisor

Division of Unintentional Injury Prevention

National Center for Injury Prevention and Control

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Background and need

- 11% of Americans experience daily (chronic) pain
- Opioids frequently prescribed for chronic pain
- Primary care providers
 - account for ~50% of opioid pain medications dispensed
 - report concern about opioids and insufficient training
- 16,000 opioid-related overdose deaths in 2013—4 x as many as in 1999, continue to increase
- About 2 million people abused or were dependent in 2013
- Existing national guidelines were published in 2010 or earlier and do not incorporate new evidence published since 2010

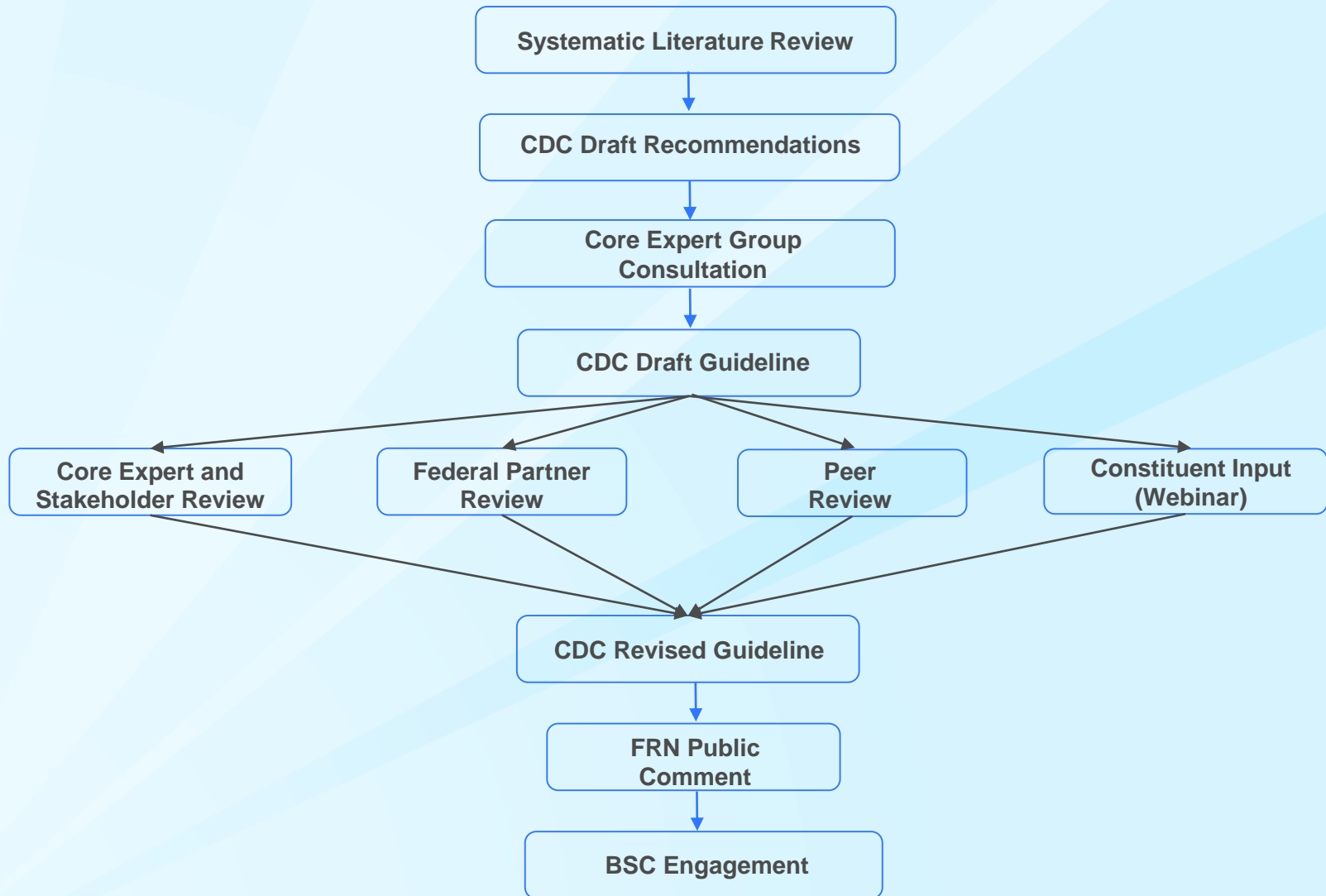
Purpose of a CDC guideline

- Support informed clinical decision making
- Help providers offer safer, more effective care for patients with chronic pain
- Help reduce misuse, abuse, and overdose from opioids
- Encourage improved communication between providers and patients about the benefits and risks of opioid therapy
- Improve provider confidence regarding when and how to use opioids in management of chronic pain
- Benefit patient health

Primary audience

Primary care providers (e.g., family physicians, internists) treating patients ≥ 18 years with chronic pain (i.e., lasting > 3 months or past time of normal tissue healing) in outpatient settings outside of active cancer treatment, palliative care, and end-of-life care

Overview of the development process



Grading of Recommendations Assessment, Development, and Evaluation (GRADE)

- Standard for guideline development
- Transparent approach for conducting systematic review, rating quality of evidence, and determining strength of recommendations
- Used by > 100 organizations (including CDC; e.g., ACIP)
- Recommendations based on:
 - Quality of evidence
 - Balance between benefits and harms
 - Values and preferences
 - Resource allocation (cost)

Definition of evidence types

- Type 1: Randomized controlled trials or overwhelming evidence from clinical studies
- Type 2: Randomized controlled trials with important limitations, or exceptionally strong evidence from clinical studies
- Type 3: Observational studies or randomized controlled trials with notable limitations
- Type 4: Clinical experience and observations, observational studies with important limitations, or randomized controlled trials with several major limitations

Recommendation categories

Category A

- Decision applies to all persons in a specified group
- Most patients should receive recommended course of action

Category B

- Decisions are made on an individual “case by case” basis
- Choices vary based on patient’s values and preferences, and specific clinical situations
- Made when advantages and disadvantages of a clinical action are more balanced

Organization of Recommendations

The 12 recommendations are grouped into three conceptual areas:

- Determining when to initiate or continue opioids for chronic pain
- Opioid selection, dosage, duration, follow-up, and discontinuation
- Assessing risk and addressing harms of opioid use

**Determining when to initiate or
continue opioids for chronic pain**

Recommendation One

Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.

Providers should only consider adding opioid therapy if expected benefits for both pain and function are anticipated to outweigh risks to the patient.

(Recommendation category: A, evidence type: 3)

Recommendation One Rationale

- Insufficient evidence to determine whether pain relief, function, or quality of life improves with long-term opioid therapy (most RCTs <6 weeks)
- Long-term opioid use for chronic pain is associated with serious risks, including abuse, dependence and overdose
- Many non-opioid therapies can improve chronic pain with less risk for harm, including exercise therapy, cognitive behavioral therapy, non-opioid pharmacologic therapies, and multidisciplinary approaches
- When opioids are used, they are more likely to be effective if combined with other approaches

*findings summarized from the clinical and contextual evidence reviews

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Recommendation Two

Before starting opioid therapy for chronic pain, providers should establish treatment goals with all patients, including realistic goals for pain and function. Providers should not initiate opioid therapy without consideration of how therapy will be discontinued if unsuccessful. Providers should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

(Recommendation category: A, evidence type: 4)

Recommendation Two Rationale

- It is difficult for providers and patients to predict whether benefits will outweigh risks of long-term opioid therapy
 - Weak evidence that some patients experience pain relief long-term
 - Inconsistent results with currently available risk stratification tools
- Medications should not be continued when harms outweigh benefits
- Establishing treatment goals in advance will help providers and patients make decisions about continuing or stopping drugs
- Pain relief, function, and quality of life are all important

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Recommendation Three

Before starting and periodically during opioid therapy, providers should discuss with patients known risks and realistic benefits of opioid therapy and patient and provider responsibilities for managing therapy.

(Recommendation category: A, evidence type: 3)

Recommendation Three Rationale

- Providers should involve patients in decisions about whether to start opioid therapy
- Many patients lack information about opioids
- Essential elements to communicate
 - Realistic expected benefits
 - Common and serious harms
 - Expectations for both patients and providers to mitigate risks

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Opioid selection, dosage, duration, follow-up, and discontinuation

Recommendation Four

When starting opioid therapy for chronic pain, providers should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

(Recommendation category: A, evidence type: 4)

Recommendation Four Rationale

- Higher overdose risk among patients initiating treatment with ER/LA opioids than among those initiating treatment with immediate release opioids
- Did not find evidence that continuous, time-scheduled use of ER/LA opioids is more effective or safer than intermittent use of immediate-release opioids

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Recommendation Five

When opioids are started, providers should prescribe the lowest effective dosage.

Providers should use caution when prescribing opioids at any dosage, should implement additional precautions when increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day, and should generally avoid increasing dosage to ≥ 90 MME/day.

(Recommendation category: A, evidence type: 3)

Recommendation Five Rationale

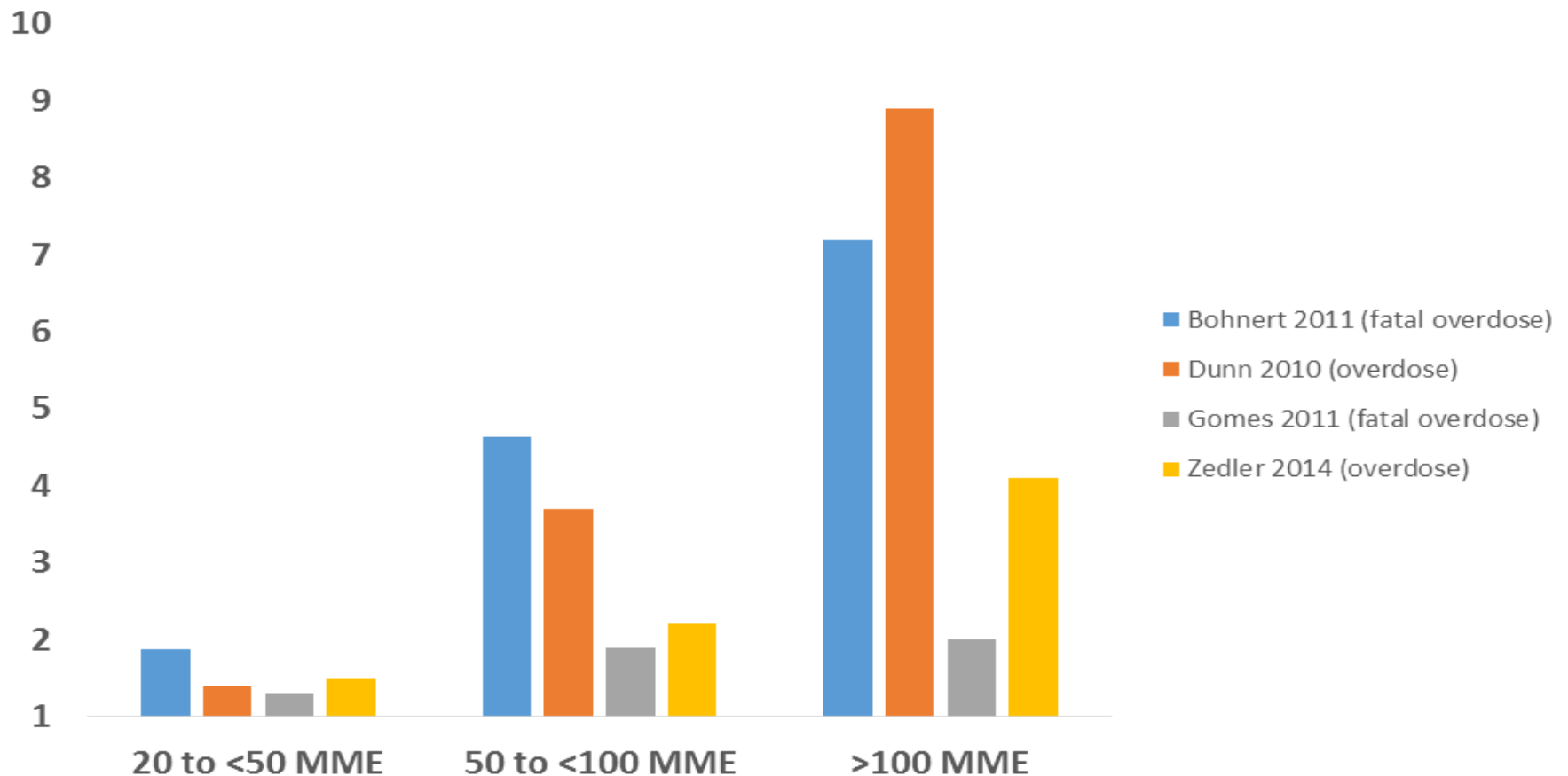
- Risks for serious harms related to long-term opioid therapy increase in a dose-dependent manner
- In a large, national VA sample, 59% of fatal overdose cases had dosages above 50 MME and 33% had dosages above 90 MME; among cases not experiencing overdose, most (76%) had dosages <50 MME; 88% had dosages <90 MME
- Benefits of high-dose opioids for chronic pain not established.
 - RCT: no difference in pain, function between more liberal dose escalation (average 52 MME at end of study) and maintenance of current dosage (average 40 MME at end of study)

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Relationship of prescribed opioid dose in MME and overdose risk

Odds ratio or hazard ratio for overdose at prescribed dosages, relative to 1 to <20 MME



Recommendation Six

Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, providers should prescribe the lowest effective dose and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three or fewer days will usually be sufficient for most nontraumatic pain not related to major surgery.

(Recommendation category: A, evidence type: 4)

Recommendation Six Rationale

- Opioid use for acute pain is associated with long-term opioid use, and greater amount of early opioid exposure is associated with greater risk for long-term use
- More than a few days of exposure significantly increases hazards
- Fewer days' supply minimizes the number of pills available for intentional or unintentional diversion
- In most cases of acute pain (e.g., acute back pain) not related to major surgery or trauma, pain severe enough to require opioids will subside within 3 days

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Recommendation Seven

Providers should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Providers should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, providers should work with patients to reduce opioid dosage and to discontinue opioids.

(Recommendation category: A, evidence type: 4)

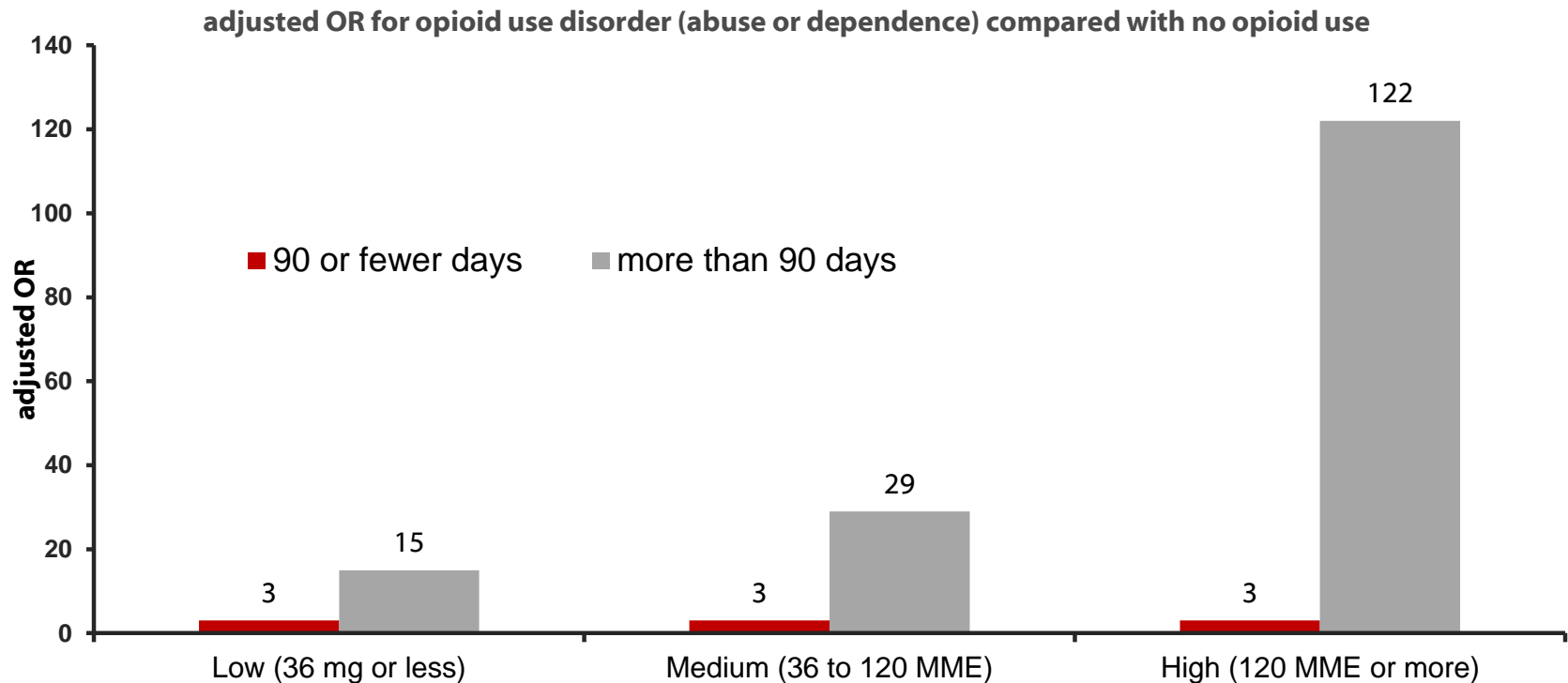
Recommendation Seven Rationale

- Risks for opioid overdose highest during 1st 2 weeks after initiation for ER/LA opioids, within 1st 3 days for methadone
- Patients who do not experience pain relief with opioids at one month are unlikely to experience pain relief with opioids at 6 months
- Continuing opioid therapy for 3 months substantially increases risk for opioid use disorder

*findings summarized from the clinical and contextual evidence reviews

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Longer durations and higher doses of opioid treatment are associated with opioid use disorder



Assessing risk and addressing harms of opioid use

Recommendation Eight

Prior to starting and periodically during continuation of opioid therapy, providers should evaluate risk factors for opioid-related harms. Providers should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, or higher opioid dosages (≥ 50 MME), are present.

(Recommendation category: A, evidence type: 4)

Recommendation Eight Rationale

- Opioids can worsen central sleep apnea and increase risk for respiratory depression and overdose
- Reduced renal or hepatic function can result in a smaller therapeutic window between safe dosages and dosages associated with respiratory depression
- Patients with mental health co-morbidities and histories of substance use disorder are at higher risk for opioid use disorder and overdose
- Community-based naloxone distribution has been associated with reduced opioid-related overdose death

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Recommendation Nine

Providers should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving dangerous combinations that put him/her at high risk for overdose. Providers should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months

(Recommendation category: A, evidence type: 4)

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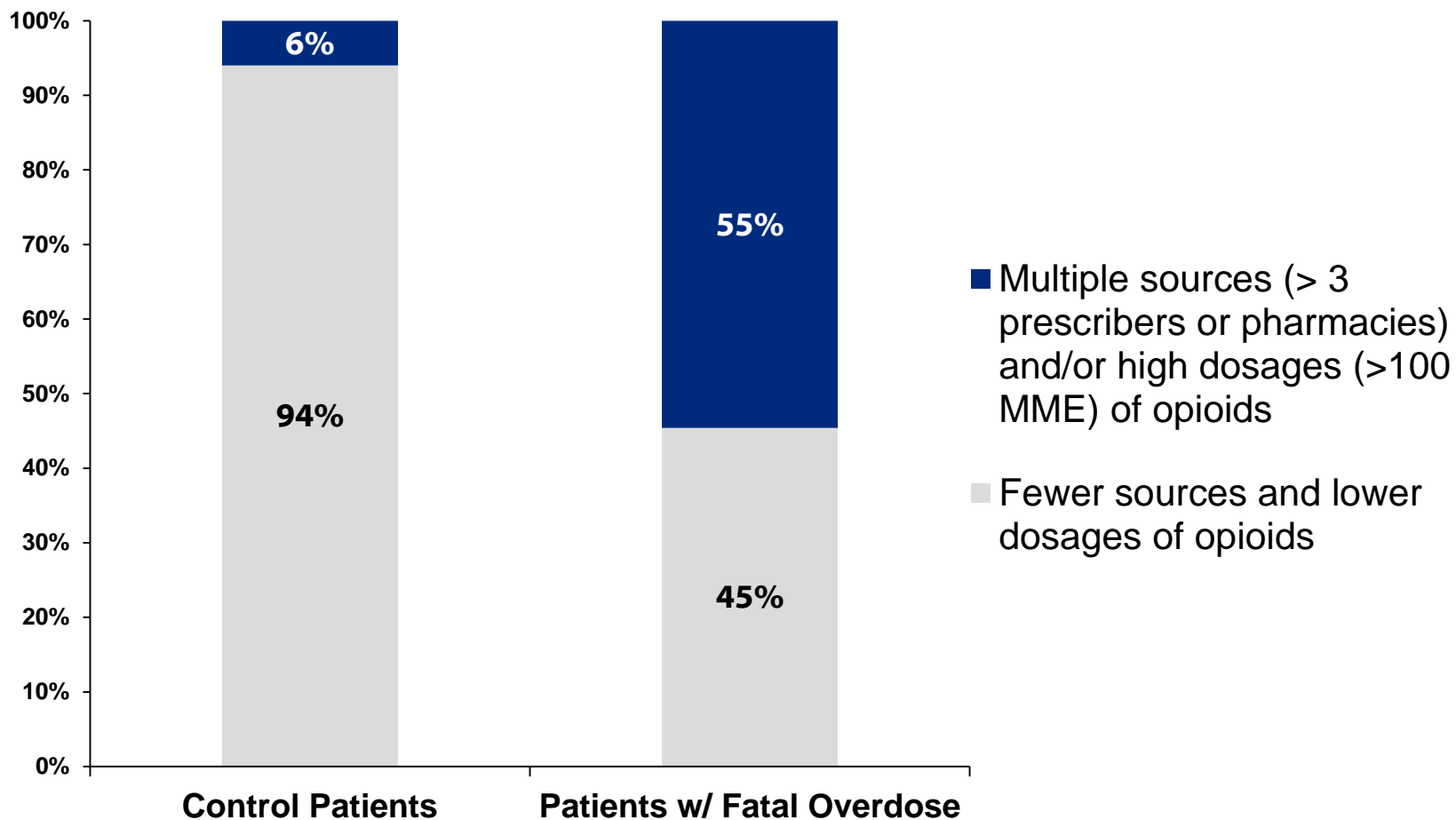
Recommendation Nine Rationale

- Most fatal overdoses are associated with
 - high total prescribed daily opioid dosages and/or
 - receipt of opioids from multiple prescribers or pharmacies
- Both of these risk factors can be assessed by reviewing PDMP data

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Majority of opioid overdose deaths associated with multiple sources and/or high dosages



Recommendation Ten

When prescribing opioids for chronic pain, providers should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs

(Recommendation category: B, evidence type: 4)

Recommendation Ten Rationale

- Urine drug tests can provide useful information about unreported drug use that can increase patients' risk for overdose, such as benzodiazepines, or heroin
- Factors influencing category B designation:
 - Cost burden for patients—not always covered by insurance
 - Test results often misinterpreted by providers

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Recommendation Eleven

Providers should avoid prescribing opioid pain medication for patients receiving benzodiazepines whenever possible.

(Recommendation category: A, evidence type: 3)

Recommendation Eleven Rationale

- Concurrent benzodiazepine and opioid prescription associated with a near quadrupling of risk for overdose death compared with opioid prescription alone (case-cohort study)
- Concurrent benzodiazepine use found in large proportions of opioid-related overdose deaths in epidemiologic case series

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Recommendation Twelve

Providers should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

(Recommendation category: A, evidence type: 3)

Recommendation Twelve Rationale

- Prevalence of opioid use disorder (previously called opioid dependence, or addiction) among primary care patients on chronic opioid therapy 3%-26%
- Buprenorphine or methadone effective in preventing relapse among patients with opioid use disorder

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